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> *"Hay-fever is an exudative catarrh of the conjunctival, nasal, and tracheo-bronchial mucous membranes, of seasonal periodicity, produced in hypersensitive individuals by the sensitizing and anaphylatoxic action of the pollen of certain plants."*—KOESSLER.

Prophylaxis and Treatment
of
Hay-Fever
with
Pollen Vaccine

With Clinical Results following the Use of Lederle's Pollen Vaccine during the seasons of 1915 and 1916.

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Hay-Fever

Its Prophylaxis and Treatment

The scientific status of the treatment of hay-fever with pollen vaccine was very completely treated in a paper entitled, "Hay Fever: The Nature of the Process and of the Mechanism of the Alleviating Effect of Specific Treatment," by Cooke, Flood and Coca, (*The Journal of Immunology,* February, 1917, p. 217) who conclude as follows:

"Assembling the available facts, clinical and experimental, relating to hay-fever, we may formulate the following conception of that form, and indeed of all forms, of natural human sensitization:

"(1) Hay fever is the clinical symptomatic expression of local hypersensitiveness. The active pollen substances are not toxins.

"(2) The hypersensitiveness is established spontaneously and never by immunological process. This has been shown in two ways: first by the observation of Dunbar, confirmed by Cooke, that individuals may be sensitive to pollens of plants that are indigenous in foreign countries and with which they have never come in contact; and secondly, by the observation of Cooke that *individuals who are naturally sensitive to one protein only can not be artificially sensitized to another protein,* either animal or vegetable.

"(3) The sensitization is not directly inherited (Cooke and Vander Veer) although the tendency to spontaneous sensitization is inherited as a dominant character.

"(4) The antibody-like substances of human sensitization are not demonstrable in the blood of sensitive persons by any of the immunity reactions. They are present in the cells of the sensitive tissues. They can not be increased artificially by the usual process of immunization.

"(5) The mechanism of the alleviating effect of specific, *i. e.,* vaccine therapy, is the same as that of desensitization in experimental anaphylaxis. The freedom from symptoms lasts as long as the respective "antigenic" substances remain in combination with the antibody-like substances in the tissues."

Historic Review of the Work on Pollen Extracts

The medical world is indebted to Dunbar (*Zur Ursache und Specifichen Heilung des Heufiebers,* Muenchen, 1903) for the exhaustive scientific proof of the specific action of pollen as the causative factor of hay-fever.

In 1911, Noon and Freeman published from Wright's laboratory in London the first scientifically conducted and controlled experiments on active immunization in hay-fever by hypodermic inoculation with pollen extract.

Noon (*The Lancet*, June 10, 1911, p. 1572) was the first to establish a Pollen Unit. He used Dunbar's method of extracting the pollen with distilled water aided by freezing and thawing several times. He defined the unit as the equivalent of one one-millionth gram of pollen.

Freeman (*The Lancet*, Sept. 16, 1911, p. 814) published a tabulated list of 20 patients inoculated with pollen extracts and recorded only one failure. Both he and Noon succeeded in materially alleviating the condition of sufferers from European or spring hay-fever by administering small doses of pollen extract.

Clowes (*Proceedings Society for Experimental Biology and Medicine,* 1913, X, 70) was the first to report a definite method of vaccination against hay-fever in this country. He adopted a method of extraction previously employed by Dunbar, consisting of repeated freezing and thawing in a 5 per cent aqueous suspension and he also used an original method which consisted of precipitating the pollen with acetone and then extracting with water.

Koessler (*Forchheimer's Therapeusis of Internal Diseases*, Vol. V, p. 671) must be given the credit for placing the method of active immunization against hay-fever on a scientific basis, for he was the first to report detailed methods of preparing pollen extracts. He subjected definite quantities of pollen to trituration and then extracted in 8.5 per cent salt solution. He adopted Noon's pollen unit and carried out immunization on 41 patients by administering the extract in accordance with a definite table of dosage which he worked out. His results corresponded very closely with those reported by the English investigators.

Researches by the Lederle Antitoxin Laboratories

The foregoing investigations established beyond doubt that desensitization with extracts of pollen was possible; and further, that by this means the onset of hay-fever could often be entirely prevented when the extract was administered prior to the usual date of the attack, and that the symptoms of hay-fever could be very materially alleviated or even cured when the extract was used after the disease manifested itself. Koessler, however, emphasized the fact *that the pollen extract was not stable and that it rapidly deteriorated in potency* after three or four weeks. He pointed out that the material to be injected must be constantly of uniform potency and that no extract of pollen which he had studied could comply with this demand if it were more than three weeks old.

Recognizing the value of the work that had been done on this subject, the Lederle Antitoxin Laboratories at this stage of the investigations took up the problem of preparing the active antigenic principle of the pollen in stable and suitable form for general distribution. *A method was perfected in the Lederle Antitoxin Laboratories of extracting the pollen which yielded a product that proved to be potent and remarkably stable. We further found that this product could be accurately standardized by immunologic methods, thereby enabling us to prove its keeping qualities.* The Lederle Antitoxin Laboratories were thus able to offer for the first time for general use (May, 1915) a uniformly potent pollen vaccine which laboratory tests showed would remain fully potent for a sufficient period to permit the complete treatment being administered.

Since then, further studies and tests have conclusively demonstrated that LEDERLE'S POLLEN VACCINE will remain fully potent without any deterioration for a long period. We can therefore now permit its being stocked by druggists throughout the country with the utmost confidence that it will retain its full potency and therapeutic value.

Another important result of the research by the Lederle Antitoxin Laboratories was in the standardization of the product. The previous work on standardization of pollen extracts was based either on the weight of the pollen used, or on a chemical analysis of the extract for its nitrogen content. These methods of standardization did not determine the antigenic strength of the extract. LEDERLE'S POLLEN VACCINE is standardized against anti-pollen serum, whereby *the active antigenic power of the vaccine is definitely determined and measured;* thus providing a uniform graduation of dosage which insures the maximum degree of protection with the minimum of reaction.

LEDERLE'S POLLEN VACCINE *is manufactured under U. S. Government License No. 17.* It is *accurately standardized* and may be used without preliminary diagnostic tests.

Clinical Results Obtained With Lederle's Pollen Vaccine

In 1915, LEDERLE'S POLLEN VACCINE was used by over 600 physicians for the prophylaxis and treatment of hay-fever. A clinical history blank was submitted to each physician, and the results of the collected data are as follows:

1. Favorable results followed as a *prophylactic* against hay-fever in *83 per cent* of the cases.
2. In the *treatment* of hay-fever, favorable results followed in *89 per cent* of the cases.
3. Marked asthmatic symptoms were associated with 55 per cent of the cases. The symptoms were relieved in 84.2 per cent of these cases.

During 1916, LEDERLE'S POLLEN VACCINE was employed by over 1500 physicians with the following results:

1. Favorable results followed as a *prophylactic* in *80 per cent* of the cases.
2. In the *treatment* of hay-fever, favorable results were obtained in *91.7 per cent* of the cases.
3. Marked asthmatic symptoms were associated with 53 per cent of the cases. These symptoms were successfully relieved in 78.5 per cent of the cases. LEDERLE'S POLLEN VACCINE was used with favorable results in 40 States of the Union: from Maine to California; and as far away as Porto Rico.

The favorable results obtained during these two consecutive years are very similar and establish conclusively the value of LEDERLE'S POLLEN VACCINE in hay-fever. The above results in the prophylaxis of hay-fever are based on the use of LEDERLE'S POLLEN VACCINE *according to our original recommendation of 15 doses* for the complete treatment.

How Favorable Results Were Manifested

Prophylaxis

When LEDERLE'S POLLEN VACCINE was used as a prophylactic, beginning about six to eight weeks before the expected attack of hay-fever, favorable results followed in that either *hay-fever did not develop*, or, in those cases in which hay-fever did develop, *the symptoms persisted for a few hours or a few days only* and were very mild in character. Even patients who had experienced *attacks of hay-fever* associated with marked asthmatic symptoms *for forty consecutive years, remained free* from both hay-fever and asthmatic symptoms.

Treatment

When used for the purpose of treating an actual attack of hay-fever, LEDERLE'S POLLEN VACCINE produced favorable results *by cutting short the attack and making the symptoms more mild.* The average number of doses required to produce marked improvement in the condition was three; while *all symptoms abated on the average after 8 doses.* In some cases the symptoms did not entirely subside until the complete treatment of 15 doses had been given.

When to Vaccinate

When LEDERLE'S POLLEN VACCINE is used as a prophylactic, best results follow by beginning the vaccine treatment about six to eight weeks before the expected attack of hay-fever, so that the treatment will be completed about three or four days before the date of the usual attack. However, the vaccine treatment may be started at any time before the onset of the disease, but the protection may not be as complete.

LEDERLE'S POLLEN VACCINE, when used for treating patients who are already suffering from hay-fever, yields excellent results. Marked improvement usually follows after the third dose; while all symptoms of hay-fever subside, on the average, after the eighth dose.

Directions for Use

LEDERLE'S POLLEN VACCINE is administered subcutaneously—usually in the upper arm at the insertion of the deltoid muscle—using the same careful asepsis as for any hypodermic injection. The correct amounts of vaccine for the various doses are supplied in individual vials serially numbered, each vial containing approximately 0.1 c.c. of the vaccine —*an amount so small that it is hardly perceptible.* Immediately before administration, the vaccine must be diluted with the sterile diluent which is furnished in a separate vial.

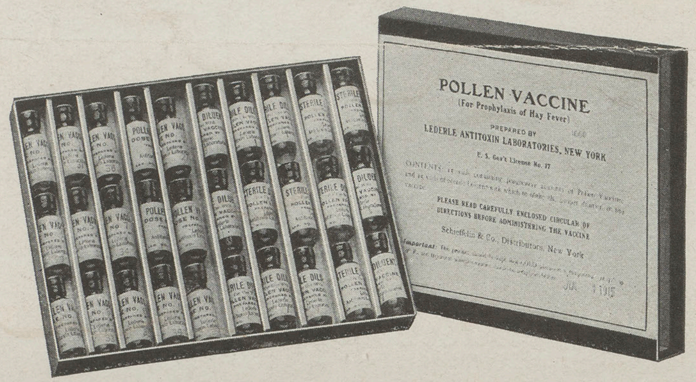
The interval between doses is usually 48 hours—a convenient plan being to administer the vaccine three times a week. A small percentage of patients (less than one per cent of the cases reported) may exhibit a hypersensitiveness to pollen protein. In such cases it may be advisable to inject only a fraction of the doses in order to prevent a reaction.

Packages

LEDERLE'S POLLEN VACCINE is supplied in the following packages:

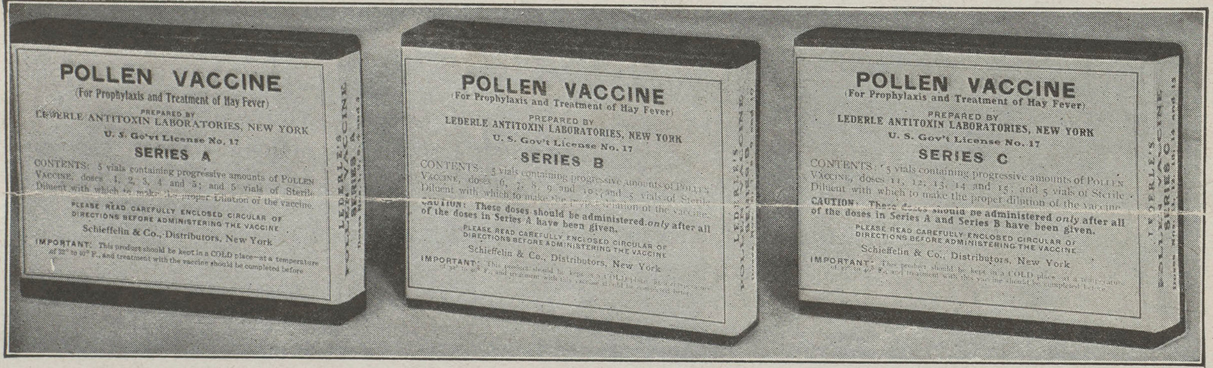
- Complete Series, containing Doses 1 to 15.
- Series A, containing Doses 1 to 5.
- Series B, containing Doses 6 to 10.
- Series C, containing Doses 11 to 15.

Full directions as to dosage and administration accompany each package.


POLLEN VACCINE
(For Prophylaxis of Hay Fever)
PREPARED BY
LEDERLE ANTITOXIN LABORATORIES, NEW YORK
U. S. Gov't License No. 17
PLEASE READ CAREFULLY ENCLOSED CIRCULAR OF DIRECTIONS BEFORE ADMINISTERING THE VACCINE
Schieffelin & Co., Distributors, New York

COMPLETE SERIES, containing Doses 1 to 15

PRICE $15.00


POLLEN VACCINE
(For Prophylaxis and Treatment of Hay Fever)
LEDERLE ANTITOXIN LABORATORIES, NEW YORK
U. S. Gov't License No. 17
SERIES A
PLEASE READ CAREFULLY ENCLOSED CIRCULAR OF DIRECTIONS BEFORE ADMINISTERING THE VACCINE
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SERIES B
CAUTION: These doses should be administered only after all of the doses in Series A have been given.
Schieffelin & Co., Distributors, New York
POLLEN VACCINE
(For Prophylaxis and Treatment of Hay Fever)
PREPARED BY
LEDERLE ANTITOXIN LABORATORIES, NEW YORK
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SERIES C
CAUTION: These doses should be administered only after all of the doses in Series A and Series B have been given.
Schieffelin & Co., Distributors, New York

SERIES A, containing Doses 1 to 5. These are the initial doses for the treatment.

PRICE $5.00

SERIES B, containing Doses 6 to 10. These doses should be administered only after all of the doses in Series A have been given.

PRICE $5.00

SERIES C, containing Doses 11 to 15. These doses should be administered only after all of the doses in Series A and Series B have been given.

PRICE $5.00